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Euglycemic diabetic ketoacidosis associated with a sodium-glucose co transporter 2 inhibitor use in a trauma patient: a case report

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Abstract

Background Sodium-glucose co-transporter 2 inhibitors (SGLT2i), like empagliflozin, are widely prescribed for managing type 2 diabetes mellitus. However, they carry a rare but serious risk: euglycemic diabetic ketoacidosis (EDKA). EDKA's atypical presentation, characterized by metabolic acidosis and ketosis despite normal blood glucose levels, often delays diagnosis, posing significant challenges in intensive care.

Case presentation We report the case of a 74-year-old female with type 2 diabetes on empagliflozin, gliclazide, and metformin. Admitted after severe trauma from a road traffic accident, she subsequently developed EDKA. This was fostered by septic shock due to methicillin-susceptible *Staphylococcus aureus* cellulitis. All home medications were discontinued. EDKA was successfully managed with fluid volume expansion, continuous intravenous insulin and dextrose infusions, resolving her metabolic derangements within five days.

Conclusion SGLT2i use is associated with a significantly increased risk of EDKA. Early diagnosis is critical due to its potential lethal consequences. Reintroducing SGLT2i in ICU patients, especially trauma patients at high sepsis risk, requires careful, daily reassessment given their unpredictable clinical course.

Keywords Trauma, Euglycemic diabetic ketoacidosis, Sodium-glucose co transporter 2 inhibitors, Sepsis shock

Background

Sodium-glucose cotransporter 2 inhibitors (SGLT2i), including empagliflozin, dapagliflozin, and canagliflozin, are an increasingly utilized therapeutic class for type 2 diabetes [1]. Recent guidelines from the American Diabetes Association and the European Association for the Study of Diabetes recommend SGLT2i as a second-line treatment for patients not achieving adequate glycemic control with lifestyle modifications and metformin [2]. These therapies are particularly indicated in patients with concomitant cardiovascular or renal comorbidities. Their mechanism of action, which inhibits glucose and sodium reabsorption in the renal proximal tubule, improves both glycemic control and cardio-renal outcomes [3, 4]. Notably, the EMPA-REG OUTCOME study demonstrated a significant reduction in cardiovascular mortality in these patient populations [5]. Furthermore, the DEFENDER TRIAL, evaluating SGLT2i in critically ill patients with organ impairment (including hemodynamic failure), reported no instances of euglycemic diabetic ketoacidosis (EDKA), suggesting their potential safety even in high-risk populations [6].

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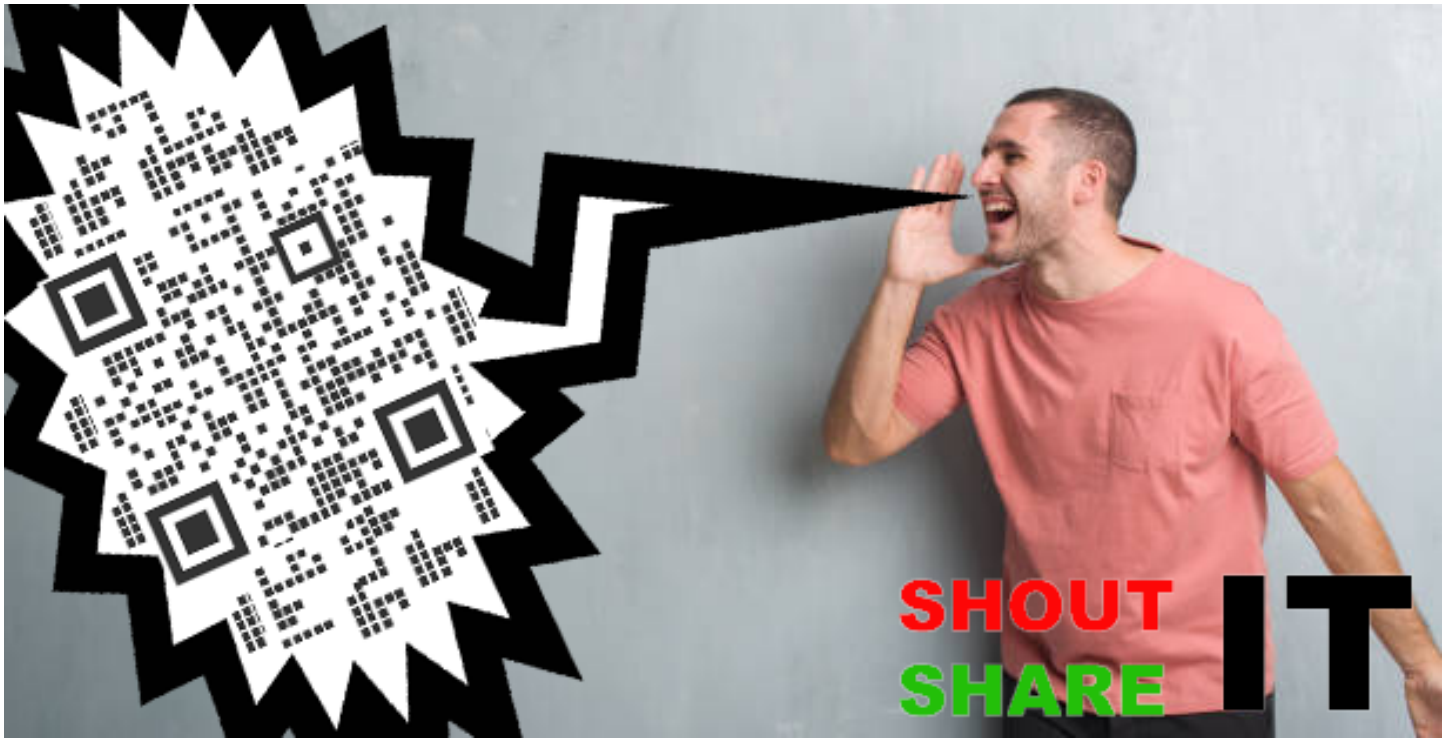
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Despite these benefits, there are increasing reports in the literature of EDKA associated with SGLT2i therapy [7–10]. Moreover, the risk of EDKA has been shown to be higher with SGLT2i compared to other oral antidiabetic agents [11].

Classically, EDKA is defined by the triad of hyperglycemia (> 13.7 mmol/L), high anion gap metabolic acidosis (pH < 7.3), and hyperketonemia or hyperketonuria [12]. However, when blood glucose levels are normal or low, as in EDKA, diagnosis becomes challenging and is often delayed [13]. The consequences of delayed diagnosis can be extremely serious, potentially leading to fatal outcomes.

Here, we report a clinical case of EDKA in a trauma patient hospitalized in intensive care unit (ICU), in whom chronic SGLT2i therapy was reintroduced. This case report adheres to the CARE guidelines for reporting clinical cases in the literature [14].

Case report

A 74-year-old female with a medical history of hypertension and type 2 diabetes mellitus was admitted to ICU following severe trauma from a road traffic accident. On admission, her home medications included empagliflozin, gliclazide, metformin, ramipril, amlodipine, and esomeprazole.

Initially, the patient presented with no hemorrhagic shock or organ failure. Her Glasgow Coma Scale (GCS) score was 14 upon arrival at the trauma center.

A computed tomography (CT) scan revealed:

- Mild traumatic brain injury with brain contusion hemorrhage and subarachnoid hemorrhage.
- Facial bone fractures.
- Thoracic trauma (Thoracic Trauma Score = 11) with a left-sided hemopneumothorax, which did not require drainage.
- American Association for the Surgery of Trauma (AAST) grade 3 traumatic splenic injury.
- Non hemorrhagic, non surgical pelvic trauma.

None of these injuries necessitated surgical intervention. An occipital scalp wound was debrided and sutured. Apart from esomeprazole, none of her long-term medications were resumed upon initial management. The patient's initial medical course was favorable. Consequently, on Day 4, oral antidiabetic medications, including empagliflozin, were reintroduced.

From Day 5, the patient developed an unexplained fever without deterioration in her general condition.

By Day 7, while awaiting discharge from the ICU, her overall condition acutely deteriorated. She presented with a decreased level of consciousness (GCS 7/15), atrial fibrillation (heart rate 150–160 bpm), hemodynamic instability (90/54 mmHg), tachypnea (25–30 breaths per minute), hyperthermia (40 °C), and facial and left arm edema.

Arterial blood gas analysis revealed severe metabolic acidosis (pH 6.99, bicarbonate 6 mmol/L, pCO2 15 mmHg, pO2 105 mmHg, base excess − 23.4 mmol/L) with a lactate concentration of 1.8 mmol/L and a glucose concentration of 13.7 mmol/L.

Management initiated for septic shock included fluid resuscitation, vasopressor therapy, and broad-spectrum antibiotics. Subsequent cranial and thoraco-abdomino-pelvic CT scans revealed dermohypodermitis of the face, secondary to an occipital skin wound infection.

Further laboratory analysis showed a serum creatinine level of 55 µmol/L, discordant with her profound metabolic acidosis. This biochemical dissociation excluded acute kidney injury as the primary etiology, prompting evaluation for alternative causes such as diabetic ketoacidosis or toxic-mediated acidosis. In this context, a plasma ketone measurement was performed, revealing a level greater than 6 mmol/L. This strongly supported a diagnosis of EDKA associated with SGLT2i use.

All oral antidiabetic drugs, including empagliflozin, were discontinued. After achieving hemodynamic stability with aggressive crystalloid fluid resuscitation and correction of hypokalemia, a continuous intravenous insulin infusion was initiated, concurrently with a 10% dextrose infusion to prevent hypoglycemia.

Microbiological analysis confirmed methicillin-susceptible *Staphylococcus aureus* bacteremia, with positive blood cultures for nearly six days. Based on the antibiogram, antibiotic therapy was adjusted, and cloxacillin was subsequently introduced. A mitral valve endocarditis, characterized by a 12 mm mobile vegetation with renal and splenic emboli, developed as a secondary complication of the bacteremia. The patient was deemed unsuitable for surgical treatment due to her head trauma, which contraindicated extracorporeal circulation.

The shock resolved after 4 days, leading to the discontinuation of norepinephrine. After 5 days of insulin therapy, the patient's acidosis resolved, and serum ketone bodies were negative. The continuous intravenous insulin infusion was then transitioned to a basal-bolus insulin regimen.

Ultimately, the clinical course of this infectious episode was favorable under well-managed antibiotic therapy for 6 weeks. The patient was transferred to a rehabilitation center after a 62-day ICU stay.

Discussion

SGLT2i-linked EDKA, though rare, can be underdiagnosed due to normal or low blood glucose levels. Misdiagnosis of this condition is extremely serious, with

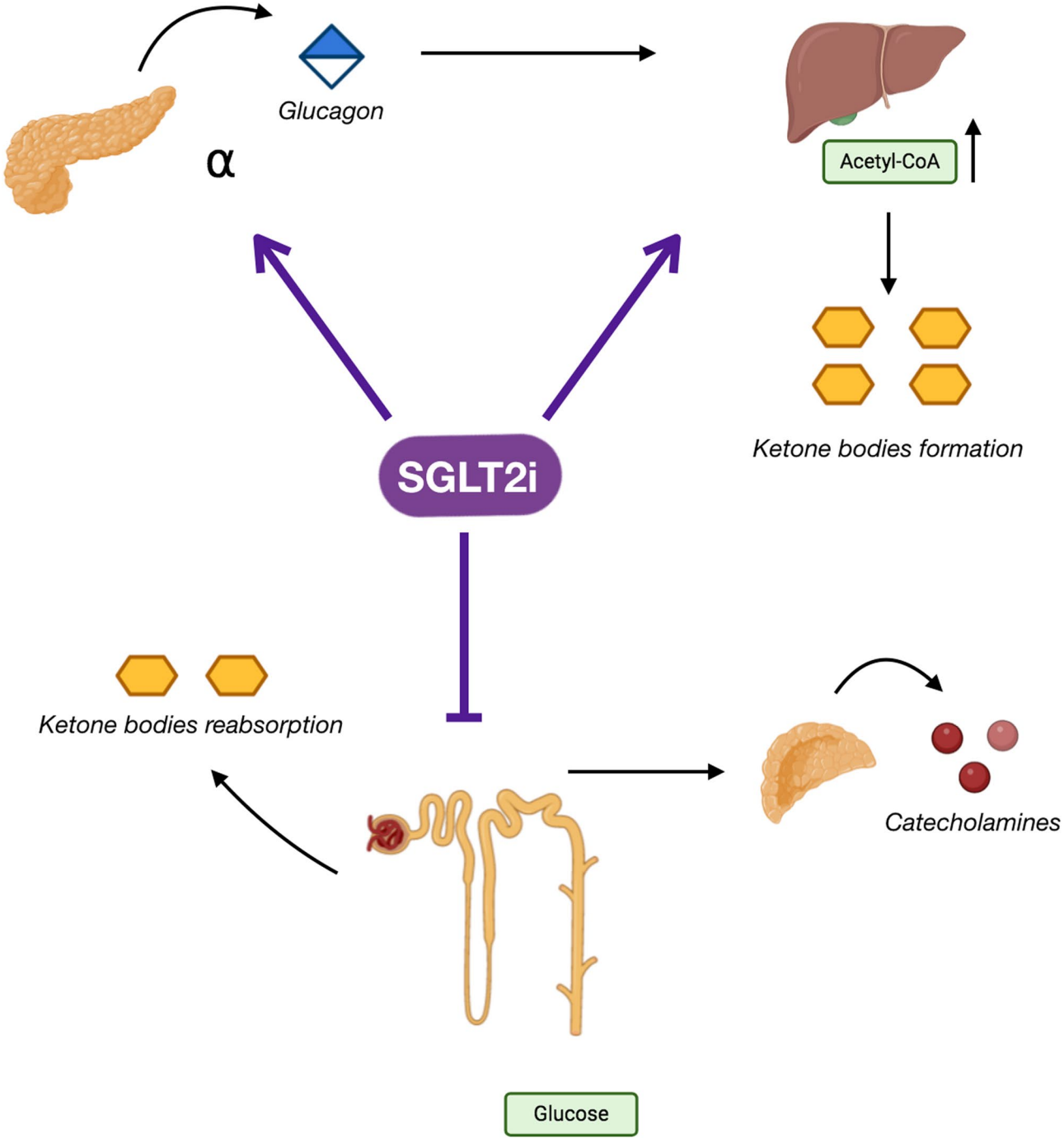

Fig. 1 Mechanism of action of the sodium-glucose co transporter 2 inhibitors. α = alpha for alpha Langerhans islets

short-term consequences including cerebral edema, ionic disorders (hypokalemia), hemodynamic failure, and acute respiratory distress syndrome; all of which can ultimately be fatal [15].

The pathophysiology of EDKA remains uncertain, but several mechanisms have been proposed (Fig. 1) [16–18]:

- SGLT2i inhibits sodium and glucose reabsorption in the renal proximal tubule, increasing glycosuria and natriuresis. This lowers blood glucose levels, reducing insulin secretion.
- Reduced insulin secretion leads to counter-regulation with increased pancreatic glucagon release. Glucagon secretion is also directly stimulated by SGLT2i in pancreatic α cells. This elevated

glucagon/insulin ratio stimulates lipolysis and free fatty acid release into circulation, which are then converted into ketone bodies via β-oxidation.
- Decreased insulin and increased glucagon levels inhibit acetyl-CoA carboxylase, promoting carnitine palmitoyl transferase-I activity in the liver and, consequently, β-oxidation.
- SGLT2i lead to increased reabsorption of ketone bodies in the proximal renal tubule.
- SGLT2i induces a negative water balance, triggering catecholamine and cortisol secretion, which further promote glucagon secretion, lipolysis, and ketone body production.

SGLT2i do not directly induce EDKA, but rather increase susceptibility to this complication when precipitating factors are present [18]. These factors are typically conditions of insulin or carbohydrate deficiency, which stimulate ketogenesis.

Literature identifies several precipitating factors that heighten the risk of EDKA in SGLT2i-treatedpatients [19]. These include a history of previous EDKA, excessive alcohol use, pre-existing diabetes (particularly insulin-dependent), female sex, body mass index ≥ 25 kg/m2, acute illness, infection or trauma, and pregnancy.

This case study underscores the critical importance of carefully managing oral antidiabetic agents, especially SGLT2i, in hospitalized ICU patients [20]. The American Diabetes Association recommends avoiding SGLT2i in cases of severe illness, prolonged fasting, and during surgical procedures [2]. Given their long elimination half-life, which allows once-daily administration [21], the metabolic disorder in our patient persisted for five days due to empagliflozin's prolonged half-life. This further supports exercising extreme caution regarding the timing of SGLT2i re-initiation in trauma patients.

Complications can arise at any point during an ICU stay, even in patients who initially show improvement. Therefore, SGLT2i should not be resumed during the ICU course without a thorough risk-benefit evaluation. Clinicians must remain vigilant when considering reintroduction, as transient improvements do not eliminate the potential for subsequent adverse events, consistent with current literature.

Conclusion

EDKA is a rare but potentially serious side effect of SGLT2i. With the increasing use of these drugs, EDKA cases are increasingly reported by healthcare professionals. Its atypical presentation with relatively euglycemic states can mislead physicians. Clinicians must remain highly vigilant and monitor ketone levels in all SGLT2i-treated patients presenting with unexplained acidosis. Delayed or missed diagnosis can lead to serious, even fatal, consequences. Therefore, SGLT2i therapy should be meticulously evaluated based on a benefit-risk assessment before reintroduction in the intensive care setting.

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Authors' contributions
OD and ML wrote the manuscript text, ML prepared the figure 1. All authors reviewed the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable. Written informed consent was obtained from the patient for publication of this case report.

Consent for publication
A consent for publication is obtained from the patient's family, as the patient was unable to provide consent.

Competing interests
The authors declare no competing interests.

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References

1. Shen T-H,et, Joel F. « utilization and impact of SLGT2 inhibitors among diabetes patients in a nationally representative survey: findings from NHANES 2013–2020 ». J Diabetes Complicat. 2023. https://doi.org/10.1016/j.jdiacomp.2023.108625.
2. Heidenreich PA, Bozkurt B, Aguilar D. etal. 2022AHA/ACC/HFSAGuideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145(18):e895–e1032. https://doi.org/10.1161/CIR.0000000000001063
3. Anker SD, Butler J, Filippatos G, EMPEROR-Preserved trial investigators. Empagliflozin in heart failure with a preserved ejection fraction. N Engl J Med. 2021;385(16):1451–61. https://doi.org/10.1056/NEJMoa2107038.
4. Wanner C, Inzucchi SE, Lachin JM. Empagliflozin and progression of kidney disease in type 2 diabetes. N Engl J Med. 2016;375(4):323–34. https://doi.org/10.1056/NEJMoa1515920.
5. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M,etal. « empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes ». N Engl J Med. 2015;373(22):211728. https://doi.org/10.1056/NEJMoa1504720.
6. Tavares CAM, Azevedo LCP, Rea-Neto Á. Dapagliflozin for critically ill patients with acute organ dysfunction: the DEFENDER randomized clinical trial. JAMA. 2024;332(5):401–11. https://doi.org/10.1001/jama.2024.10510.
7. de Velasco G. María Isabel Sánchez-Molina acosta, et María matilde Toval fernández. 2021. « diabetic euglycemic ketoacidosis induced by oral antidiabetics type SGLT2i ». EJIFCC32(1):10510.
8. Diaz-Ramos A, Eilbert W, etDiego Marquez. 2019.«Euglycemicdiabicko-acidosisassociatedwithsodium-glucosecotransporter-2inhibitoruse:acasereportandreviewoftheliterature».International Journal of Emergency Medicine12(septembre):27.https://doi.org/10.1186/s12245-019-0240-0
9. Hedary A, Melder L, Micah Pippin. « A case of euglycemic diabetic ketoacidosis associated with a Sodium-Glucose Cotransporter-2 (SGLT2) inhibitor ». Cureus. 2024;16(12):e75399. https://doi.org/10.7759/cureus.75399.

10. Bteich F, Daher G, Kapoor A, Charbek E, Kamel G. Post-surgical euglycemic diabetic ketoacidosis in a patient on empagliflozin in the intensive care unit. Cureus. 2019;11(4):e4496. https://doi.org/10.7759/cureus.4496. Published 2019 Apr 18.
11. AdoMoumouni A. « SGLT-2 inhibitors and ketoacidosis: A disproportionality analysis in the world health organization's adverse drug reactions database ». Fundam Clin Pharmacol. 2018;32(2):21626. https://doi.org/10.1111/fcp.12334.
12. Wysham C, Bindal A, Levrat-Guillen F, Kostadinova D, etYeesha Poon. 2025.«ASystematicLiteratureReviewontheBurdenofDiabicKoacidosisinType-2DiabesMellitus».Diabes,Obesity&Mabolism,mars.https://doi.org/10.1111/dom.16282
13. Schutte B, Savage K, Merwin M, Morris M, Geringer R, Dilsaver DB, Plambeck RW, etNikhil Jagan. 2025 « euglycemic diabic koacidosis: rising incidence, diagnostic delays, and the impact of SGLT2 inhibitors in hospitalized patients ». J Hosp Med.https://doi.org/10.1002/jhm.70015
14. Gagnier JJ, Kienle G, Altman DG. The CARE guidelines: consensus-based clinical case reporting guideline development. BMJ Case Rep. 2013;2013:bcr2013201554. https://doi.org/10.1136/bcr-2013-201554. Published 2013 Oct 23.
15. Westerberg DP. Diabetic ketoacidosis: evaluation and treatment. Am Fam Physician. 2013;87(5):337–46.
16. Ogawa W, Kazuhiko Sakaguchi. « euglycemic diabetic ketoacidosis induced by SGLT2 inhibitors: possible mechanism and contributing factors ». J Diabetes Invest. 2016;7(2):13538. https://doi.org/10.1111/jdi.12401.
17. Palmer BF,et, Deborah J. « euglycemic ketoacidosis as a complication of SGLT2 inhibitor therapy ». Clin J Am Soc Nephrology: CJASN. 2021;16(8):128491. https://doi.org/10.2215/CJN.17621120.
18. Malherbe J. DamienduCheyron,etXavierValette.2025.«UnderstandingtheDisease:EuglycemicKetoacidosiswithSGLT2Inhibitors».IntensiveCareMedicine.https://doi.org/10.1007/s00134-025-07806-3
19. Bamgboye A, Collier Andrew. Predisposing factors for the development of diabetic ketoacidosis with lower than anticipated glucose levels in type 2 diabetes patients on SGLT2-inhibitors: a review. Eur J Clin Pharmacol. 2021;77(5):651–7. https://doi.org/10.1007/s00228-020-03051-3.
20. Garcia B, Ostermann M, Matthieu Legrand. « how to manage Sodium-Glucose Cotransporter-2 inhibitors in the critically ill patient?? ». Intensive Care Med. 2025;51(1):14345. https://doi.org/10.1007/s00134-024-07704-0.
21. Wright EM. SGLT2 Inhibitors. Physiol Pharmacol Kidney360. 2021;2(12):2027–37.

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